Oral Sessions
Sepsis care: 0001–0005

0001

EFFECTIVENESS OF AN EDUCATIONAL PROGRAM TO REDUCE SEPSIS MORTALITY IN SEVERAL HOSPITALS IN SPAIN

C. Salazar Ramirez[1], I. Bellido Estévez[2], M. V. de la Torre-Prados[1]

[1]H. U. Virgen de la Victoria, Intensive Care Unit, Malaga, Spain, [2]Medical School Malaga, Pharmacology and Clinical Therapeutic, Malaga, Spain

INTRODUCTION. To determine the effectiveness of an educational program based on Surviving Sepsis Campaign guidelines to reduce sepsis mortality in several hospitals in Spain.

METHODS. Eleven Spanish ICUs, in the South of Spain (Andalucia) were included in a prospective study. A multicentric study realised during 2005 and 2006. We determined the rate of compliance of the resuscitation bundle (first 6 h) and the management bundle (first 24 h) during 2 months before the educational program and 4 months after the educational program.

RESULTS. Three hundred and thirty patients were enrolled in this analysis: severe sepsis (29.4%) or septic shock (70.6%) admitted in intensive care units. There were no significant differences between the groups with respect to base-line characteristics and severity of illness measured by the Acute Physiology and Chronic Health Evaluation II were similar for both groups. Patients characteristics were as follows: age, 62 (60, 63) years; APACHE II score, 21 (20, 22). The main sources of infection were: lung (36.1%), abdomen (28.1%) and UTI (11%). CVP and Svc02 monitoring, antibiotics, fluid resuscitation, mechanical ventilation, vasopressors, inotropes, corticosteroides, and rhAPC were included in the educational program. The patients in the after EP period had measured more Svc02 (36.2 vs. 15.5%), CVP (45.7 vs. 39.9%) and lactate (27.7 vs. 23.2%) All patients received broad-spectrum antibiotics, patient in the after group received more corticosteroids (35 vs. 25%), a lower lactate (3.8 vs. 5.19 mmol/l), blood culture (47.4 vs. 37.5%), were more likely to receive intravenous fluids of >20 ml/kg body weight before vasopressor administration (38 vs. 36%), patient in the after group were less likely to require vasopressor (43 vs. 47%). In the after EP period these patients had a shorter length of stay in intensive care (238 vs. 280 h, we reduced the length in 15.1%) and shorter hospital length of stay (688 vs. 719 h). Mortality in ICU pre-EP was 43.8% and after-EP was 31.6%. The percentage of compliance with 6-h and 24-h bundle in the after-EP increased, respectively (9.85%, $P < 0.01$ and 8.86%), total compliance was also 46.62%.

CONCLUSIONS. Our study found the implementation of a standardized order set for the management of septic shock was associated with an important decreased of the mortality (12.2%), improving early and accurate diagnosis and increasing the use of appropriate treatment and interventions.

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0002

CONVERTING GUIDELINE TO PRACTICE: EXPERIENCE IN IMPLEMENTING SEPSIS RESUSCITATION BUNDLE FOR SEVERE SEPSIS AND SEPTIC SHOCK IN THE EMERGENCY DEPARTMENT

Z. Wang[1]

[1]Peking University 3rd Hospital, Beijing, China

INTRODUCTION. Patients with severe sepsis and septic shock have a mortality rate of 30–50%. It is well recognized that sepsis outcomes are directly related to delays in diagnosis and treatment. The aim of this study was to compare the mortality of two group patients before and after implementing sepsis resuscitation bundle in the emergency department.

METHODS. This is a prospective study. The studied population included severe sepsis and septic shock patients entered in the Surviving Sepsis Campaign (SSC) data base, who were admitted to the emergency department of an urban tertiary care medical center during Sep 2008–April 2009. They were divided into two groups based on the admission time (Group 1: Sep 2008–Dec 2008, baseline survey of real practice in sepsis therapy before creating a protocol. Group 2: Jan 2009–April 2009, creating a protocol implementing sepsis resuscitation bundle in sepsis therapy). Acute physiology and chronic health evaluation (APACHE II) scores and in-hospital mortality were compared.

RESULTS. One hundred and twenty-five (125) severe sepsis and septic shock patients were included, mortality was 60.5% in group 1 and 51% in group 2 ($P < 0.05$). No significant differences were noted among two groups with respect to age, gender, lactic acid level, median APACHE II score. Sepsis resuscitation bundle compliance was 1% in group 1 and 9% in group 2 ($P < 0.05$).

CONCLUSIONS. The results revealed a mortality benefit after implementing sepsis resuscitation bundle in the emergency department. Sepsis guideline could reliably be implemented better in real-world clinical practice if creating a protocol.

0003

EFFECTIVENESS OF TREATMENTS FOR SEVERE SEPSIS: A PROSPECTIVE MULTICENTER OBSERVATIONAL STUDY IN SPANISH ICUS

R. Ferrer Roca[1], Edusepsis Study Group

[1]Sabadell Hospital, CSPT. UAB. CIBER-ER, Sabadell, Spain

INTRODUCTION. The improvement of the compliance of the Surviving Sepsis Campaign (SSC) guidelines was able to reduce mortality (Edusepsis study, Ferrer et al. JAMA 2008).

OBJECTIVE. To analyze the impact on hospital mortality of severe sepsis treatments included in the SSC guidelines in a prospective multicenter observational study.

METHODS. We included all consecutive adult patients with severe sepsis or septic shock from the 77 participating intensive care units (ICU) from the database of the Edusepsis study. Treatments evaluated were those included in the SSC bundles: Early administration of broad spectrum antibiotics (time from severe sepsis presentation to antibiotic administration: first hour, 1–3 h, 3–6 h, previous antibiotic or no antibiotic administered in the first 6 h), fluid challenge of a minimum of 20 ml/kg of crystalloid (or colloid equivalent) in the event of hypotension and/or lactate >36 mg/dl, low-dose steroids in the event of persistent hypotension despite fluid resuscitation and/or lactate >36 mg/dL, and drotrecogin alfa (activated) for multiorgan failure. The primary outcome measure was hospital mortality. The effectiveness of each of the four treatments was estimated by using Propensity Scores (PS) in the sub-sample where the treatment was indicated. All risks factors for mortality, therapeutic goals of the SSC bundles (CVP ≥8 mm Hg, $ScvO_2$ ≥70%, blood glucose <150 mg/dl without hypoglycemia and inspiratory plateau pressure <30 cmH_2O) and the other treatments were included in the PS models. In order to assess the balancing of covariates between treated and untreated groups in each PS quintile we adopted a fully exhaustive approach comparing all the covariates for treated and untreated groups within each quintile, along with a graphical approach plotting box plots of the estimated PSs for treated and untreated patients within each quintile. For each assessed treatment, to take into account potential residual imbalances in the final model, we included all the covariates that showed a statistically significant difference between treated and untreated groups in some quintile and APACHE II.

RESULTS. Of 2,796 patients, 1,164 (41.6%) died before hospital discharge. The mean age of all subjects was 62.2 years, mean APACHE II was 21, mainly were male (61.4%) and predominantly with medical septic conditions (62.2%); pneumonia (26.5%) was the most common infection. Two therapeutic interventions were associated with lower hospital mortality: administration of broad spectrum antibiotic treatment in the first hour of severe sepsis (OR 0.65; 95% CI 0.49–0.88; $P = 0.005$) and administration of drotrecogin alfa (activated) in multiorgan failure (OR 0.59; 95% CI 0.42–0.85; $P = 0.004$).

CONCLUSION. Early administration of antibiotics in all patients and drotrecogin alfa (activated) in the most severe patients are able to reduce severe sepsis mortality.

0004

EFFECT OF SEPSIS STAGING-DIRECTED THERAPY (SSDT) IN THE TREATMENT OF SEVERE SEPSIS AND SEPTIC SHOCK

S.-H. Wang[1], C. W. Lam[1], T.-S. Wei[2], S.-J. Kou[3], H.-C. Chang[3], S. H. Lin[1]

[1]Changhua Christian Hospital, Critical Care Division of Surgical Department, Changhua, Taiwan, Republic of China, [2]Changhua Christian Hospital, Department of Medical Education and Research, Changhua, Taiwan, Republic of China, [3]Changhua Christian Hospital, Surgical Department, Changhua, Taiwan, Republic of China

BACKGROUND. Surviving Sepsis Campaign (SSC) management guidelines are crucial to the survival of severe sepsis and septic shock. Sepsis-related Organ Failure Assessment (SOFA) score is an important tool for severity of sepsis related organ failure. Based on the SSC guideline and SOFA score, we develop a Sepsis Staging-Directed Therapy (SSDT) system to guide sepsis bundle treatment on severe sepsis and septic shock.

METHODS. In a single center, surgical intensive care unit, prospective cohort study, we classified sepsis into five stages which stage I was uncomplicated, stage II and stage III were severe sepsis, and stage IV and stage V were septic shock. We surveyed severe sepsis and septic shock patients before and after SSDT implementation. The primary end point was the mortality rate 28 days after presentation of severe sepsis or septic shock.

RESULTS. A total of 557 patients (298 patients were historical control group, and 259 patients were SSDT intervention group) were enrolled and included in analysis. There were significant difference between SSDT intervention group and historical control group in 28-day mortality rate (18.9 and 30.9%, respectively; $P = 0.001$), in-hospital mortality rate (27.0 and 44.3%, respectively; $P < 0.001$). The multivariate logistic regression analysis showed that SOFA score and SSDT were independent prognostic predictors of 28-day mortality (OR = 0.79; 95% CI = 0.67–0.93; $P = 0.005$ and OR = 0.42; 95% CI = 0.23–0.75; $P = 0.004$, respectively) and in-hospital mortality (OR = 0.80; 95% CI = 0.69–0.94; $P = 0.006$ and OR = 0.32; 95% CI = 0.18–0.57; $P < 0.001$, respectively).

CONCLUSIONS. Stratified sepsis to a sepsis stage system according to SOFA score is an innovative try and useful for clinical therapy intervention. The SSDT effectively improved the outcome of severe sepsis and septic shock. We supposed that SSDT system could be widely implemented in a multicenter, multi-country for further research.

0005

THE EFFECT OF TRANSCUTANEOUS ELECTRIC MUSCLE STIMULATION ON LOSS OF MUSCLE MASS IN ICU PATIENTS WITH SEPTIC SHOCK

J. B. Poulsen[1], K. Møller[1], H. Kehlet[2], A. Perner[1]

[1]Rigshospitalet, University of Copenhagen, Department of Intensive Care, Copenhagen, Denmark, [2]Rigshospitalet, University of Copenhagen, Section for Surgical Pathophysiology, Copenhagen, Denmark

BACKGROUND. ICU admission for septic shock is associated with loss of muscle mass and functional limitations [1]. We investigated the effect of early transcutaneous electric muscle stimulation (TEMS) on muscle mass of the quadriceps muscle in septic patients.

METHODS. We included seven adult patients with septic shock within 72 h of diagnosis. Exclusion criteria were diabetes, infection in or trauma to the lower extremities, corticosteroid treatment equivalent to prednisolone dose >1 mg/kg/day, predicted ICU stay of <7 days and clinical conditions that constituted a contraindication for computed tomography (CT). Patients were randomised to unilateral TEMS of the quadriceps muscle. The contra-lateral leg served as control. Stimulation was done daily for 60 min in seven consecutive days via carbon 5 × 5 cm and 5 × 9 cm pad electrodes and using a battery-powered stimulator (Danmeter, Elalpha 3000) programmed to evoke contractions at 33 Hz at intervals of 3 s separated by 6-s intervals. The distal electrode was placed over the motor point, which was identified as the point with the lowest threshold to produce a visible twitch in response to an electrical pulse. Each day the threshold value was determined as the current resulting in barely visible muscle contraction. The stimulating current was set at 50% above the threshold current, corresponding to moderate training intensity. All patients underwent CT scanning of both thighs before and after 7 days of TEMS. The quadriceps muscles were manually delineated on the CT slides, and muscle volumes were automatically calculated after 3-D reconstruction. The patients were otherwise treated according to standard protocols for resuscitation, antibiotics, source control, sedation and nutrition. All patients were ventilated and confined to bed-rest throughout the study period as a consequence of their critical illness.

RESULTS. Mean age and SAPS II of the patients were 69 years (SD 6) and 55 (SD 9), respectively. During the 7-day study period, muscle volume in the stimulated muscle decreased by mean 17% (SD 15, $P = 0.02$, compare to baseline by paired t test) corresponding to a rate of 2.4%/day. Control muscle volume decreased by 14% (SD 13, $P = 0.03$), i.e. 2.0%/day. There was no difference in the mean changes in muscle volume between the stimulated and control leg ($P = 0.17$ by paired t test).

CONCLUSION. We observed a marked decrease in quadriceps volume in the first week of intensive care for septic shock. However, this loss of muscle mass was unaffected by TEMS applied for 60 min/day.

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0007

HIGH FREQUENCY OSCILLATION AND TRACHEAL GAS INSUFFLATION FOR SEVERE ACUTE RESPIRATORY DISTRESS SYNDROME: RESULTS FROM A SINGLE-CENTER, PHASE II, RANDOMIZED CONTROLLED TRIAL [NCT00416260]

S. Malachias[1], S. Kokkoris[1], S. Zakynthinos[1], S. D. Mentzelopoulos[1]

[1]University of Athens, Intensive Care Medicine, Athens, Greece

INTRODUCTION. Animal data supports the use of high-frequency oscillation (HFO) in acute respiratory distress syndrome (ARDS). Preceding clinical comparisons of HFO and conventional mechanical ventilation (CMV) were inconclusive. Combined HFO and tracheal-gas insufflation (TGI) improves oxygenation versus standard HFO and lung-protective CMV [1], thus potentially enabling reduction of ventilation pressures. We hypothesized that intermittent HFO-TGI may improve respiratory function and impact survival in patients with early and severe ARDS, ventilated with pressure- and volume-limited, lung-protective CMV (plateau-pressure target $\leq$30 cmH_2O, tidal volume = 5.5–7.5 mL/kg predicted body weight).

METHODS. We performed a prospective, randomized, unblinded, parallel-group, controlled trial in a 37-bed university intensive care unit. We studied a total of 54 patients with early ($\leq$72 h in duration) ARDS and severe oxygenation disturbances (PaO_2/FiO_2 of <150 mm Hg for >12 consecutive hours with positive end-expiratory pressure $\geq$8 cmH_2O). Patients were randomly assigned to the intervention (HFO-TGI) group ($n = 27$) or the control (CMV) group ($n = 27$). HFO-TGI group received sessions of HFO-TGI (whenever PaO_2/FiO_2 <150 mmHg for >12 consecutive hours), followed by lung-protective CMV. CMV group received lung-protective CMV.

RESULTS. Within days 1–8 post-randomization, HFO-TGI group received 116 sessions of HFO-TGI (duration-range: 6–48 h). During days 1–8, oxygenation, plateau-pressure and respiratory compliance were improved in HFO-TGI group versus CMV group ($P \leq 0.001$). Within days 1–60, HFO-TGI versus CMV group had more ventilator-free days, and more days without respiratory, coagulation, liver, renal, and any organ failure ($P = 0.047$–0.003); barotrauma incidence and length of hospital stay were similar. HFO-TGI group versus CMV group had improved survival to days 28 and 60 ($P = 0.02$–0.03), but not to hospital discharge (16/27, 59.3% vs. 9/27, 33.3%; $P = 0.10$).

CONCLUSION. In severe ARDS, intermittent HFO-TGI (interspersed with CMV) improves respiratory function and short-term clinical course, but not in-hospital mortality, length of hospital stay, or barotrauma.

GRANT ACKNOWLEDGEMENT. Supported in part by the Thorax Foundation.

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Acute lung injury: Innovative therapies: 0006–0010

0006

SYSTEMATIC TWO-DAY MUSCLE RELAXANTS COURSE IN THE EARLY PHASE OF SEVERE ACUTE RESPIRATORY DISTRESS SYNDROME. A MULTICENTER RANDOMIZED CONTROLLED TRIAL

L. Papazian[1], J.-M. Forel[2], A. Gacouin[3], G. Perrin[2], S. Jaber[4], J.-M. Arnal[5], D. Perez[6], J.-M. Seghboyan[7], J.-M. Constantin[8], P. Courant[9], A. Roch[2], ACURASYS study group

[1]Hôpital Sainte-Marguerite, Réanimation Médicale, Marseille, France, [2]Hôpital Sainte-Marguerite, Marseille, France, [3]Hôpital Pontchaillou, Rennes, France, [4]Hôpital Gui de Chauliac, Montpellier, France, [5]Hôpital Font-Pré, Toulon, France, [6]Hôpital Jean Minjoz, Besançon, France, [7]Hôpital Ambroise Paré, Marseille, France, [8]Hôpital Hôtel Dieu, Clermont-Ferrand, France, [9]Centre Hospitalier, Avignon, France

INTRODUCTION. The use of neuromuscular blocking agents (NMBA) remains controversial, empirical and no clear recommendation is available. In the context of a proven reduction of mortality of ARDS when a lung-protective MV (limitation of tidal volume and plateau pressure) is applied, muscular paralysis induced by NMBA in a lung-protective ventilation should be considered.

OBJECTIVES. We conducted a multicenter randomized, controlled trial to determine the efficacy and safety of NMBA.

METHODS. Patients receiving endotracheal mechanical ventilation for hypoxemic acute respiratory failure were eligible if the following criteria were met for no more than 48 h before enrollment: PaO_2:FIO_2 <150 mm Hg at time of enrollment while a PEEP of at least 5 cmH_2O and a tidal volume of 6–8 ml/kg were applied, recent appearance of bilateral pulmonary infiltrates consistent with edema, and no clinical evidence of left atrial hypertension (pulmonary-capillary wedge pressure <18 mm Hg, when available). After obtaining a Ramsay sedation score of VI and optimizing the ventilator settings according to the ventilator procedure, cisatracurium or placebo were administered during 48 h.

RESULTS. We screened 1,326 patients at 20 French centers during the study period. 177 patients were included in hte NMBA group, and 162 to the control group. The two groups were similar with respect to demographic characteristics, reason for ICU admission, cause of lung injury, and measures of the severity of illness at baseline. However, in the NMBA group, the mean PaO_2:FiO_2 was significantly lower ($P = 0.03$). The 90-day mortality rate was 31.6 percent (95% CI, 25.2–38.8%) in the group treated with NMBA and 40.7% (95% CI, 33.5–48.4%) in the placebo group ($P = 0.08$), for an absolute difference of −9.1% (95% confidence interval for the difference between groups, −19.3 to 1.1%). The Cox regression model (group assignment, SAPS 2, plateau pressure and PaO_2:FiO_2 ratio) yielded an adjusted hazard ratio for death at 90 days for the NMBA group compared with the control group of 0.68 (95% CI, 0.48–0.98) ($P = 0.04$).The 28-day mortality rate was 23.7% in the group treated with NMBA and 33.3% in the group who received placebo (RR, 0.71 [95% CI, 0.51–1.00], $P = 0.05$). The NMBA group had significantly more ventilator-free than the placebo group during the first 28 days as well as at 90 days. As compared with the placebo group, the NMBA group had significantly more failure-free days for other organs than lung during the first 28 days (3.6 days, $P = 0.002$). There were no difference concerning the incidence of muscular weakness evaluated by the MRC score either at day 28 or at ICU discharge. There were more patients from the control group (11.7%) than from the NMBA group (5.1%) who developed an episode of pneumothorax ($P = 0.03$).

CONCLUSIONS. A systematic short course of NMBA improved outcome in severe ARDS.

0008

PULMONARY VASCULAR LEAKAGE AFTER COMBINED BURN AND SMOKE INHALATION INJURY IS REDUCED BY CONTINUOUS INTRAVENOUS INFUSION OF RECOMBINANT HUMAN ANTITHROMBIN DUE TO INHIBITION OF NEUTROPHIL ACTIVATION

S. Rehberg[1], Y. Yamamoto[1], D. L. Traber[1], Y. Zhu[1], C. Jonkam[1], L. Sousse[1], K. Bansal[1], M. O. Maybauer[1], D. M. Maybauer[1], L. D. Traber[1], P. Enkhbaatar[1]

[1]The University of Texas Medical Branch, Anesthesiology, Galveston, United States

INTRODUCTION. Antithrombin (AT) was shown to inhibit endotoxin-induced endothelial adherence of neutrophils by binding at the Syndecan-4 receptor [1].

OBJECTIVES. We hypothesized that AT reduces the transition of neutrophils into the lymph and thereby pulmonary vascular permeability. Therefore, this randomized, controlled study was designed to investigate the effects of a continuous, intravenous infusion of recombinant human antithrombin (rhAT) on pulmonary lymph neutrophil count and flow as well as pulmonary function in an established ovine model of combined burn and smoke inhalation injury.

METHODS. Female sheep ($n = 9$) were instrumented for chronic hemodynamic monitoring. After 5 days of recovery, a tracheostomy as well as a 40% total body surface area 3rd degree cutaneous burn and smoke inhalation injury (48 breaths of cold cotton smoke <40°C) were performed under deep anesthesia. Sheep were then randomly assigned to receive either an i.v. infusion of 6 U kg^{-1} h^{-1} rhAT ($n = 4$) or only the vehicle (normal saline; $n = 5$). All sheep were mechanically ventilated and fluid resuscitated during the 48 h-study period. The rhAT treatment was started 1 h after injury. Permeability index was calculated according to the formula: lymph flow*lymph protein/plasma protein. Data are expressed as mean ± SE.

RESULTS. Baseline (BL) values and carboxy hemoglobin after smoke inhalation did not differ between groups. While AT plasma levels decreased to 66% of BL in the control group, rhAT treatment kept AT plasma levels 5–10% above BL value. Compared to control animals, rhAT decreased mean pulmonary artery pressures from 12 h on (26 ± 1 vs. 30 ± 1 mmHg), reduced pulmonary shunt fraction (28 ± 8 vs. 47 ± 3% at 48 h) and attenuated the decrease in PaO_2/FiO_2 ratio (288 ± 72 vs. 135 ± 16 mmHg at 24 h; $P < 0.05$ each). Starting at 9 h, lung lymph flow (4 ± 1 vs. 27 ± 5 mL/h), pulmonary protein flux (13 ± 3 vs. 69 ± 7 mg/h) and permeability index (4 ± 2 vs. 21 ± 2 mL/h) were significantly lower than in the control group ($P < 0.01$ each). The neutrophil count was markedly reduced in rhAT treated animals compared to control after 24 h (42 ± 23% of BL vs. 192 ± 52% of BL; $P = 0.047$) and 48 h (50 ± 22% of BL vs. 330 ± 64% of BL; $P = 0.014$). In addition, cumulative positive net fluid balance was lower in the rhAT (780 ± 750 mL) than in the control group (4457 ± 408 mL; $P = 0.003$).

CONCLUSIONS. Continuous intravenous infusion of rhAT reduces pulmonary vascular permeability and improves pulmonary function after combined burn and smoke inhalation injury. The inhibition of neutrophil transition into the lung lymph might represent a potential mechanism of action. Notably, systemic vascular leakage as represented by the cumulative fluid balance was also reduced in rhAT treated animals.

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0009

NON INVASIVE VENTILATION (NIV) BY HELMET FOR TREATMENT OF HYPOXEMIC ACUTE RESPIRATORY FAILURE (ARF): PRESSURE SUPPORT (PS) VS. NEURALLY ADJUSTED VENTILATORY ASSIST (NAVA)

G. Cammarota [1], R. Costa[2], C. Blando[1], F. Longhini[1], D. Colombo[1], R. Vaschetto[1], G. Spinazzola[2], F. Della Corte[1], G. Conti[2], P. Navalesi[1]

[1]University of Eastern Piedmont, SCDU Anestesia e Rianimazione, Novara, Italy, [2]Università Cattolica del Sacro Cuore, Anestesia e Rianimazione, Rome, Italy

INTRODUCTION. NIV can be applied in PS mode by means of a helmet. The helmet is less efficient than the face-mask in decreasing inspiratory effort and may worsen patient-ventilator synchrony (P-Vsyn). NAVA is a new form of assistance where the ventilator is driven by diaphragm electrical activity (EAdi). Respect to PS, NAVA has been shown to improve P-Vsyn in intubated patients and healthy volunteers undergoing NIV.

OBJECTIVES. Physiologic comparison between PS and NAVA in delivering NIV by helmet.

METHODS. We studied 10 patients with hypoxemic ARF. NIV was set in PS according to patient's requirements. During NAVA, PEEP remained unchanged and the NAVA gain was set to achieve the same inspiratory pressure applied in PS. Three 30-min trials (PS1, NAVA, PS2) were performed. Airway pressure (Paw) and EAdi were recorded for the last 5 min of each trial. Respiratory rate (RR), inspiratory (TI) and expiratory (TE) time, inspiratory (DelayTRi) and expiratory (DelayTRe) trigger delays were determined from Paw and EAdi signals. The time in which the ventilator supported the contracting diaphragm (Tsync) was also calculated. At the end of each trial arterial blood gases (ABGs) were measured. Data are reported as mean ± SD.

RESULTS. ABGs did not significantly change throughout the 3 trials. Ventilator TI and TE were 0.67 ± 0.12 s in PS1, 1.09 ± 0.34 s in NAVA and 0.65 ± 0.10 s in PS2 ($P < 0.0001$), and 2.22 ± 0.99 s in PS1, 1.71 ± 0.59 s in NAVA and 2.00 ± 0.58 in PS2 ($P = 0.031$), respectively. DelayTRi was 0.31 ± 0.13 s in PS1, 0.13 ± 0.05 s in NAVA and 0.36 ± 0.12 s in PV2 ($P < 0.0001$). Tsync was 0.59 ± 0.30 s in PS1, 0.79 ± 0.34 s in NAVA and 0.54 ± 0.29 s in PS2 ($P = 0.0019$). RR and DelayTRe were not different between trials.

CONCLUSIONS. Compared to PS, NAVA improved P-Vsyn without affecting ABGs and RR.

0010

RESPIRATORY SYSTEM RESPONSE TO EXCESSIVE RESPIRATORY MUSCLE UNLOADING DURING NEURALLY ADJUSTED VENTILATORY ASSISTANCE (NAVA) IN PATIENTS UNDER WEANING

G. Ferreyra[1], L. Appendini[2], L. Barberis[1], C. Burzio[1], L. Del Sorbo[1], F. Racca[1], M. Pizzio[1], L. Mascia[1], V. M. Ranieri[1]

[1]University of Turin, Anesthesiology and Critical Care, Turin, Italy, [2]Fondazione Salvatore Maugeri, Pneumology, Veruno, Italy

BACKGROUND. NAVA is an assisted ventilatory mode that generates pressure in the airways proportionally (with variable gain) to the electrical activity of the diaphragm (EAdi). We aimed to assess the physiological response to increasing gain levels of NAVA on diaphragm unloading in patients under weaning.

METHODS. Fourteen intubated, mechanically ventilated patients (71.5 ± 10 years old) on NAVA ventilation entered the study. Tidal volume (V_T), peak airway pressure (Paw_{peak}), EAdi expressed as percentage of its maximum (Edi/Edi_{max}), inspiratory (PTPes) and diaphragm (PTPdi) muscle effort were continuously measured throughout the procedure. NAVA gain was progressively increased by 0.1 $cmH_2O/\mu V$ every minute until Paw_{peak} reached 40 cmH_2O.

STATISTICS. Comparisons within groups: paired *t* test; comparisons between groups: unpaired *t* test. Significance was set at $P < 0.05$.

RESULTS. V_T and Paw_{peak} initially increased significantly with increasing NAVA gain in all patients. Subsequently, V_T and Paw_{peak} remained stable (plateau phase) due to decreases of EAdi inversely proportional to the progressive increases of NAVA gain. In each patient a NAVA gain threshold ($NAVA_H$) was reached (2.3 ± 1.3 $cmH_2O/\mu V$), above which V_T and Paw_{peak} increased over the plateau phase values (see Table 1). In six patients, EAdi remained stable above $NAVA_H$ ($EAdi_S$), while in the remaining eight patients EAdi even increased above plateau phase values ($EAdi_I$). In this latter condition, inspiratory flow increased to levels known to elicit a positive feedback on the respiratory drive (Younes J Appl Physiol 89: 481, 2000).

TABLE 1

Parameters	EAdi.S group		EAdi.I group	
	Plateau Phase	NAVA.H	Plateau Phase	NAVA.H
Pawpeak (cmH_2O)	22.1 ± 6	25.4 ± 7†	22.5 ± 5	31.8 ± 6.6†
VT (ml)	550 ± 110	617 ± 100†	540 ± 80	740 ± 340†
Flow (L/m)	0.75 ± 0.11	0.85 ± 0.07†	0.88 ± 0.21	1.19 ± 0.28*†
EAdi (%)	20% ± 9%	21 ± 9%	26 ± 12%	37 ± 14% *†
PTPdi (cm H_2O s/min)	35.7 ± 52.5	32.3 ± 46.5	85.7 ± 41.9	115 ± 61.4 †

Mean ± SD. *$P < 0.05$, NAVA.H between groups; †$P < 0.05$, NAVA.H versus Plateau Phase within groups

CONCLUSIONS. We conclude that in patients under weaning: (1) downregulation capabilities of respiratory drive are impaired when NAVA gain is above the patient's $NAVA_H$ gain threshold; (2) reflexes activated by high inspiratory flow above $NAVA_H$ increase EAdi, further contributing to increase the pressure applied to the airways. On the clinical point of view, NAVA gains forcing pressure and V_T to exceed plateau phase values and causing high inspiratory flow (above 1 L/s) must be avoided.

Fluid management: 0011–0015

0011

PROSPECTIVED RANDOMIZED CONTROLLED TRIAL COMPARING PERIOPERATIVE FLUID MANAGEMENT METHODS ON MAJOR LUNG SURGERY: PRELIMINARY RESULTS

A. Pasqualetto[1], A. Sabaté Pes[1], I. Camprubì Sociats[1], E. Boza Hernandez[1], A. Madrid Crespo[1]

[1]Hospital Universitario de Bellvitge, Anesthesiology, Barcelona, Spain

Improvements in the perioperative management of the patients undergoing pulmonary resections have reduced postoperative complication rates steadily in the last several decades. However, postresection respiratory failure, particulary ARDS, remains a major cause of morbidity and mortality, with a variable incidence of 2–5% and a mortality of 45–50%. The aetiology of postoperative acute lung injury (PALI) is not all over clear, even if the high concentration of protein in the edema fluid and delayed presentation suggest this is an inflammatory mediated process, exacerbated by excessive fluid administration and changes in pulmonary vascular permeability.

We analyzed if guiding intraoperative and postoperative fluid management by an algorithm based on optimizing the global end-diastolic volume index (GEDVI) and normalizing the extravascular lung water (EVLWI) reduces the need of inotropic and vasopressor support, the incidence of postoperative complications and the ICU stay.

DESING AND SETTING. Single-centre clinical prospective randomized study including 50 patients undergoing major lung resection surgery monitored with PiCCO 2 Pulsion Systhem (PiCCO 2 Group, P2G), compared with a control group of 50 patients monitored with IBP and CVP (CVPG). A standardized anaesthetic protocol was used during surgery for both groups.

RESULTS. In the P2G, hemodynamics goals were: GEDVI: 650–800 ml/m^2, EVLWI: 3–7 ml/kg, CI: 2.5–3.5 $l/min/m^2$, SVRI: 1,700–2,400 dynes s cm^{-5} m^2; in the CVPG, hemodynamics targets were: PAM >70 mmHg, CVP: 6–10 mmHg. The preliminary results suggest fewer administration of vasopressors and inotropics in the P2G; they received similar volume of colloids and crystalloids, without difference on the renal function outcome. The time until achieving criteria for ICU discharged was shorter in the P2G, with fewer incidence of postoperative pulmonary edema, ARDS and pneumonia.

CONCLUSIONS. Guiding fluid therapy by an algorithm based on a GEDVI and an EVLWI targets, leads to a shortened and reduced use of vasopressors, catecholamines, mechanical ventilation, and ICU stay in patients undergoing major lung resection surgery.

0012

INFUSION OF BALANCED 6% HES 130/0.4 REDUCES PERICAPILLARY EDEMA FORMATION IN THE MYOCARDIUM OF ENDOTOXEMIC SHEEP

C. Ertmer[1], S. Rehberg[1], G. Köhler[2], T. G. Kampmeier[1], C. Höhn[1], A. Morelli[3], B. Bollen Pinto[1], M. Lange[1], H. Van Aken[1], M. Westphal[1]

[1]University of Muenster, Department of Anaesthesiology and Intensive Care, Muenster, Germany, [2]University of Muenster, Department of Pathology, Muenster, Germany, [3]University of Rome 'La Sapienza', Department of Anesthesiology and Intensive Care, Rome, Italy

In the presence of hypovolemia, colloid infusion may reduce the amount of fluid needed for resuscitation as compared to crystalloids. In addition, balanced solutions as compared to saline-based solutions, may reduce the sodium and chloride load and therefore prevent metabolic acidosis. However, the impact of specific colloid preparations on organ function and microcirculation is still unclear. The purpose of the present study was to compare the effect of balanced crystalloids, as well as balanced and saline-based 6% HES 130/0.4 on myocardial microcirculatory edema formation in ovine endotoxemic shock.

Thirty-five awake sheep were subjected to incremental doses of endotoxin (started at 5 ng/kg/min and doubled every hour) until mean arterial pressure (MAP) fell below 65 mmHg. Thereafter, fluid resuscitation was initiated to maintain central venous pressure at 8–12 mmHg and pulmonary arterial occlusion pressure at 12–15 mmHg. In sheep allocated to the colloid groups, either balanced (Volulyte® 6%, $n = 10$) or saline-based HES (Voluven® 6%, $n = 10$) was infused until the maximum dose of 50 mL/kg was reached. In the crystalloid group ($n = 10$), a balanced, isotonic crystalloid (Jonosteril®) was infused to achieve goal values. The control group ($n = 5$) received no volume resuscitation. In all groups norepinephrine was titrated to achieve a MAP ≥65 mmHg. After 4 h of treatment, sheep were anesthetized, intubated and thoracotomized. Thereafter, multiple 1 mm^3 samples of left ventricular myocardium were extracted from the beating heart. Samples were immediately prepared for transmission electron microscopic evaluation of capillary area and edema formation. Data are given as median (25; 75% range).

Capillary area was higher in the resuscitated groups as compared to the control group. Capillary area [μm^2]: Control, 25 (20; 37); Crystalloid, 39 (26; 53); Balanced HES, 33 (26; 47); Saline-based HES, 45 (31; 68); $P < 0.001$).

Edema formation was highest in the crystalloid and lowest in the balanced HES group. Edema area [μm^2]: Control, 39 (26; 57); Crystalloid, 101 (76; 132); Balanced HES, 15 (5; 37); Saline-based HES, 72 (43; 120); $P < 0.001$.

The ratio of capillary to edema area was highest in the balanced HES and lowest in the crystalloid group. Ratio capillary/edema area [%]: Control, 66 (45; 120); Crystalloid, 35 (27; 48); Balanced HES, 271 (83; 750); Saline-based HES, 54; (36; 120); $P < 0.001$.

The present study provides evidence that balanced 6% HES 130/0.4 may reduce myocardial pericapillary edema formation in ovine endotoxemic shock as compared to crystalloids or saline-based HES.

0013

FLUIDS AFTER CARDIAC SURGERY (FACS): RESUCITATION WITH COLLOIDS VERSUS CRYSTALLOIDS

S. Magder[1], B. Potter[1], D. Fergusson[2], B. de Verennes[1]

[1]McGill University, Medicine, Montreal, Canada, [2]University of Ottawa, Medicine, Ottawa, Canada

RATIONAL. Colloids solutions are frequently used for volume resuscitation but their role is still controversial. We argue that the failure to find an advantage for colloids over crystalloid solutions is because protocols have not used appropriate physiological end-points and are not flow-based. Accordingly, we used a randomized double blind trial to compare the use of a pentastarch (HES) (MW 260 Kd) versus 0.9% saline (Sal) for volume resuscitation following cardiac surgery. The primary end-point was the use of catecholamines between 8:00 and 9:00 the morning after surgery for this is when the decision is made to discharge patients from the ICU.

METHODS. All patients undergoing elective cardiac surgery were eligible. Consent was obtained prior to surgery but randomization occurred postoperatively. Exclusion criteria included excessive bleeding, presence of intra-aortic balloon pump, absence of pulmonary artery catheter and unstable hemodynamics. Triggers for fluid were cardiac index (CI) <2.2 l/min/m^2, mean blood pressure or systolic pressure less than the target set by treating physicians, central venous pressure (CVP) <3 mmHg, or urine output <20/ml/h. In this nurse driven protocol blinded boluses were 250 ml and the patients were assessed as being volume responsive by assessing the CI and CVP after every bolus. When not volume responsive catecholamines were started and tapered up or down based on an algorithm. The maximum dose of study fluid was 1 l. An additional 500–750 of HES was used to prime the bypass circuit in the OR for all patients.

RESULTS. There were 119 HES and 118 Sal who received fluid. An additional 26 did not require fluid. Between 8:00 and 9:00, 13 (10.9%) HES and 34 (28.8%) Sal were on catecholamines for a relative risk reduction (RR) of 0.38 and confidence interval (CI) of 0.21, 28.8, $P = 0.001$. There was also less total catecholamine use and less time on catecholamines and a lower fluid balance (−656, CI −1203, −108, $P = 0.02$). Important secondary endpoints were a reduction of pneumonia/mediastinal infections in the HES (RR = 0.2, CI 0.04, 0.89, $P = 0.03$), reduction of cardiac pacing (RR = 0.23, CI 0.07, 0.78) and a tendency for less returns to the unit (RR 0.5, CI 0.22, 1.11, $P = 0.09$). On the safety side, there was one death in each group (1.7%). There was no difference in renal function in the two groups; 16% in each reached RIFLE risk or greater and only one in each group required dialysis. There was no significant increase in use of red blood cells but there was a significant increase in the use of plasma in HES.

SUMMARY. In this flow-based protocol, HES use significantly reduced catecholamine use the morning after surgery and showed trends to better outcome parameters with no negative effects on renal function. (ClinicalTrial.gov identifier NCT00337805).

0014

EFFECTS OF ALBUMIN ADMINISTRATION ON ACID-BASE BALANCE IN HYPOALBUMINEMIC PATIENTS

K.-M. Lee[1], D.-K. Kim[1], W.-K. Kwon[1], N. S. Woo[1]

[1]Konkuk University Hospital, Anesthesiology and Crit Care Med, Seoul, Korea, Republic of

INTRODUCTION. Compensatory acid-base changes occur as a part of normal acid-base homeostasis in response to the abnormalities of strong ion difference or $PaCO_2$. There is a respiratory compensation in response to primary disturbances in the strong ion difference and controlled renal compensation in response to primary disturbances of the $PaCO_2$. Hypoproteinemia and hperproteinemia by themselves may cause metabolic alkalosis and acidosis, respectively. However, the compensatory response to the change of blood protein concentration is not clear.

OBJECTIVES. This study was performed to evaluate the effects of albumin administration on acid-base balance in hypoproteinemic patients.

METHODS. We studied 31 adult hypoalbuminemic (albumin concentration less than 3.0 g/dL) patients who admitted to surgical ICU after receiving cardiovascular surgery. Twenty-one patients were enrolled to the Non-AKI (non-acute kidney injury) group and ten patients were enrolled to the AKI group. Following inclusion criteria of AKI were used: an abrupt (within 48 h) reduction in kidney function currently defined as an absolute increase in serum creatinine of either ≥0.3 mg/dL or a percentage increase of ≥50% (1.5 fold from baseline) or a reduction in urine output (documented oliguria of <0.5 mL/kg/h for >6 h. Patients were excluded if younger than 18 years, in shock state (mean arterial pressure less than 60 mmHg), receiving transfusion, or hemodiafiltration. We administered intravenously 100 ml of 20% albumin solution for 10 h. Patients were blood sampled from radial artery at baseline, 1 day after the albumin administration (Day 1), and 2 days after the administration (Day 2). We measured serum albumin concentration, chemistry values, and blood gas values. All data are expressed as mean ± SD. Mann–Whitney test and Friedman test were used for statistical analysis.

RESULTS. Albumin concentrations increased in both groups with the administration of albumin (Table 1). The pH was not changed significantly in both groups. Albumin administration decreased Cl^- and increased SID in Non-AKI group and these findings were not observed in AKI group. $PaCO_2$ was lower in AKI than Non-AKI on Day 1.

TABLE 1 CHANGES OF MEASUREMENTS

		Baseline	Day 1	Day 2
Albumin concentration (g/DL)	Non-AKI	2.61 ± 0.29	3.04 ± 0.30	2.97 ± 0.38
	AKI	2.60 ± 0.70	3.00 ± 0.30	3.18 ± 0.26
$PaCO_2$ (mmHg)	Non-AKI	30.7 ± 6.1	31.4 ± 4.2	32.5 ± 4.7
	AKI	30.8 ± 5.6	29.2 ± 7.4	31.4 ± 8.9
SID (mEq/L)	Non-AKI	35.5 ± 3.5	37.8 ± 3.0	38.1 ± 3.4
	AKI	38.2 ± 4.1	37.9 ± 3.6	41.7 ± 5.1
Cl^- (mEq/L)	Non-AKI	108.5 ± 4.4	106.0 ± 3.8	104.5 ± 5.1
	AKI	112.1 ± 7.5	112.0 ± 5.9	109.7 ± 3.8

CONCLUSIONS. These data suggest that the change of albumin concentration accompanies metabolic compensation with Cl^- regulation. Albumin administration may develop acidosis in renal dysfunction patients if they are depressed in ventilatory function.

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0015

TRANSFUSION OF STORED LEUCODEPLETED RED BLOOD CELLS CAUSES CARDIAC, PULMONARY AND RENAL DYSFUNCTION AND INJURY

N. N. Patel[1], H. Lin[1], C. Jones[1], P. Ray[2], T. Toth[3], P. Sleeman[1], R. Cardigan[4], G. D. Angelini[1], G. J. Murphy[1]

[1]University of Bristol, Bristol Heart Institute, Bristol, United Kingdom, [2]North Bristol NHS Trust, Department of Anaesthesia, Bristol, United Kingdom, [3]North Bristol NHS Trust, Department of Histopathology, Bristol, United Kingdom, [4]NHS Blood and Transplant Centre, Cambridge, United Kingdom

INTRODUCTION. Clinical studies have demonstrated associations between allogenic red blood cell (RBC) transfusion and organ dysfunction, particularly acute kidney injury (AKI) and transfusion associated lung injury (TRALI), however, causality has not been established and doubts remain as to the potential toxicity of RBC transfusion. The aim of this study was to determine whether transfusion has a causal effect on the development of AKI and TRALI in a large animal experimental model and to determine the changes that occur in stored porcine SAG-M RBC units and how closely they parallel those of stored human RBCs.

METHOD. Adult White-Landrace pigs (50–70 kg, $n = 20$) were randomised in a 1:1 ratio to either RBC transfusion or sham procedure. Perfusion pressure, central venous filling pressure and hydration were standardised. Endpoints included serial functional and biochemical measures of cardiac, pulmonary and renal injury. All pigs were recovered for 24 h prior to organ harvest and histological assessment of injury, inflammation and endothelial activation.

RESULTS. Transfused pigs received 1,000 ml (4 units) of cross-matched allogenic leucodepleted RBC stored in SAG-M preservative for 42 days. Accumulation of toxic metabolites within the supernatant as well as cellular changes showed considerable homology to those measured in SAG-M stored human RBC units. RBC Transfusion elicited AKI manifest by a 14% reduction in creatinine clearance (mean difference 36.1 (95% CI 3.5–68.8) ml/min, $P = 0.03$), a 46% reduction in free water clearance (mean difference 32.3 (95% CI 4.0–60.7) ml/min, $P = 0.04$) and a 69% increase in the urinary protein/creatinine ratio (mean difference 14.6 (95% CI 1.8–27.4) mg/mmol, $P = 0.03$) when compared to controls at 24 h. RBC transfusion resulted in a 69% reduction in the intra-renal ATP/ADP ratio (mean difference 4.16 (95% CI 1.03–7.30) nmoles/mg, $P = 0.02$) and a 48% reduction in nitric oxide bioavailability (mean difference 27.4 (95% CI 0.14–54.64) mmoles, $P = 0.05$). RBC transfusion also caused lung injury manifest by a 10% reduction in lung compliance (mean difference 2.5 (95% CI 0.3–4.7) ml/cmH_2O, $P = 0.03$) and a 20% increase in inspiratory airway resistance (mean difference 1.7 (95% CI −0.1 to 3.4) cmH_2O/L/s, $P = 0.06$), and cardiac injury manifest by a 9-fold increase in serum troponin (mean difference 0.19 (95% CI 0.01–0.36), $P = 0.04$) when compared to controls at 24 h. Transfusion resulted in significant changes in renal tubular morphology with marked renal tubular dilatation and vacuolation. RBC transfusion was associated with endothelial injury as evidenced by reduced excretion of urinary nitric oxide.

CONCLUSION. Transfusion of stored leucodepleted RBCs causes AKI, lung injury and myocardial injury. Endothelial dysfunction may be a pathophysiological mechanism. Modification of stored RBC prior to transfusion may reduce the incidence of organ dysfunction.

Severe infections 1: 0016–0020

0016

IN VITRO EVALUATION OF THE MALLINCKRODT SEALGUARD ENDOTRACHEAL TUBE

A. Myers[1], P. Morgan[1], A. Toner[1], M. Scott[1]

[1]Royal Surrey County Hospital, Guildford, United Kingdom

INTRODUCTION. Ventilator associated pneumonia (VAP) has an attributable mortality of 15–40% [1]. The endotracheal (ET) tube cuff forms a seal to enhance positive pressure ventilation and prevent aspiration. Folds form following inflation that allow continuous microaspiration [2]. New cuff design and material has been used in Mallinckrodt SealGuard Evac ET tubes. There is minimal work investigating the impact of tube agitation or secretion viscosity on cuff performance.

OBJECTIVES. To compare how secretion viscosity and agitation affect performance of Mallinckrodt Hi-Lo® Evac ET tubes with polyvinyl chloride cuff and Lanz pressure regulating valve (HiLo), and Mallinckrodt SealGuard Evac (SG) ET tubes (polyurethane cuff). Viscous fluid was used to represent saliva, the main component of secretions resting above the ET tube cuff in intubated patients.

METHODS. A universal specimen container (internal diameter 21 mm) was used to represent a trachea. A clean, dry "trachea" was intubated with sizes 7.0, 8.0, and 9.0 Hi-Lo and SG tubes. Cuffs were inflated to 30 cmH_2O, the minimum pressure required to create a seal. 2 ml of Methylene Blue diluted in saline or as a viscous solution (50% KY jelly), was introduced above the cuff. Time was measured from the introduction of fluid to the first drop passing below the cuff (T1), and all fluid leaking past the cuff (Tc). This was repeated three times in each size then repeated again with agitation (30 s movement in a single plane at 2 Hz every 5 min). A limit of 1 h was set to reflect intervals in subglottic secretion drainage. If leakage was incomplete in 1 h the volume of fluid leaking past the cuff was recorded.

RESULTS. (Table 1)

CONCLUSIONS. Viscosity affects performance of ET tubes and both types perform better with viscous fluid. SG performed better than HiLo but agitation reduces seal integrity. At size 7.0, the SG ET tube provided a good seal until agitation was applied. Due to the small area of cuff in contact with the "trachea", agitation resulted in rapid and complete leak. If this is reflected in clinical practice, the Sealguard tube may help reduce VAP but its effectiveness is reduced with ET movement and inappropriate tube size selection.

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TABLE 1 LEAKAGE AROUND SEALGUARD AND HILO ET TUBES

ET tube type and size	T1 non-viscous without agitation	T1 non-viscous with agitation	Tc non-viscous without agitation	Tc non-viscous with agitation	T1 viscous without agitation	T1 viscous with agitation	Tc viscous without agitation	Tc viscous with agitation
SG 7.0	46 min	5 min	Incomplete leak at 1 h (1.2 ml)	5 min 14 s	no leak	5 min	no leak	5 min 10 s
HiLo 7.0	<10 s	<10 s	<10 s	<10 s	<10 s	<10 s	<10 s	<10 s
SG 8.0	25 min	9 min	Incomplete leak at 1 h (1.0 ml)	Incomplete leak at 1 h (1.2 ml)	No leak	No leak	No leak	No leak
HiLo 8.0	34 s	37 s	4 min 41 s	49 s	45 s	<10 s	3 min	<10 s
SG 9.0	5 min	4 min 40 s	Incomplete leak at 1 h (0.5 ml)	Incomplete leak at 1 h (1 ml)	No leak	No leak	No leak	No leak
HiLo 9.0	<10 s	<10 s	16 s	<10 s	32 s	<10 s	2 min 15 s	<10 s

0017

ENTEROCOCCUS FAECIUM INFECTIONS IN A SURGICAL INTENSIVE CARE UNIT IN A GREEK HOSPITAL

A. Larentzakis[1], H. Markogiannakis[1], P. Drimousis[1], A. Xanthaki[2], M. Toutouza[2], E. Samara[1], N. Pachylaki[1], E.-M. Theodoraki[1], D. Theodorou[1], K. G. Toutouzas[1], S. Katsaragakis[1]

[1]Hippokrateion Hospital, Athens Medical School, University of Athens, Surgical Intensive Care Unit, 1st Department of Propaedeutic Surgery, Athens, Greece, [2]Hippokrateion Hospital, Department of Microbiology, Athens, Greece

OBJECTIVE. To identify and evaluate the clinical features of patients with *Enterococcus faecium* infections in our Surgical Intensive Care Unit (SICU).

METHODS. Data for all patients hospitalized in our SICU are prospectively collected in a database. Data for cases developing ICU-acquired infections by *E. faecium* between 2001 and 2007 were retrieved and analyzed.

RESULTS. During the 7-year study period, 1,255 patients were hospitalized in the SICU, 287 (22.8%) of whom suffered from an ICU-acquired infection. Among the latter, 28 sustained an *E. faecium* infection (9.8% of the patients with an infection and 2.3% of the total population) and composed our study group. Mean age of the patients with an *E. faecium* infection was 69.4 ± 5.8 years and APACHE II score 21.9 ± 5.4 (women: $n = 19$, 67.8%). The underlying surgical pathology (hospital admission diagnosis) was gastrointestinal cancer ($n = 14$, 50%), acute peritonitis ($n = 4$, 14.4%), bowel obstruction ($n = 2$, 7.1%), acute pancreatitis ($n = 2$, 7.1%), gastrointestinal tract hemorrhage ($n = 2$, 7.1%), acute cholangitis ($n = 2$, 7.1%), penetrating abdominal trauma ($n = 1$, 3.6%) and superior artery embolism ($n = 1$, 3.6%). All cases underwent operative treatment, with 11 (39.3%) of them having one or more reoperations. Twelve patients (42.8%) underwent intestinal surgery, 6 (21.4%) esophageal/gastric surgery, 4 (14.4%) biliary tract operative procedures/cholecystectomy, 3 (10.7%) had pancreatic surgical procedures and 3 cases (10.7%) liver surgery. Bloodstream infections ($n = 18$, 64.3%) and surgical site infections ($n = 8$, 28.6%) constituted the most common infection sites. The isolated microorganisms exerted high resistance to the majority of antimicrobial agents apart from linezolid (sensitivity: 100%); susceptibility to teicoplanin (64%) and vancomycin (61%) was also particularly low. Mean SICU and hospital stay was 33 ± 5.2 and 40.8 ± 6.4 days, respectively. Complication rate of these patients following *E. faecium* infection was 92.8% ($n = 26$) while 24 (85.7%) presented at least one organ/system failure. Septic shock was the most frequent complication ($n = 21$, 75%) followed by respiratory failure ($n = 19$, 67.8%), renal failure ($n = 18$, 64.3%), cardiac failure ($n = 17$, 60.7%), thrombocytopenia ($n = 11$, 39.3%), coagulopathy ($n = 11$, 39.3%), hepatic failure ($n = 7$, 25%), arrhythmias ($n = 7$, 25%), hypernatremia ($n = 6$, 21.4%), hypercalcemia ($n = 4$, 14.4%), peritonitis ($n = 2$, 7.1%) and hemorrhage ($n = 2$, 7.1%). Mortality of patients who developed an ICU-acquired E. faecium infection was 71.4% ($n = 20$), which was significantly higher than mortality of all other SICU patients sustaining ICU-acquired infections caused by other microorganisms (45.3%, $P = 0.001$).

CONCLUSIONS. *Enterococcus faecium* infections are a significant problem in SICUs due to high associated multiresistance, morbidity and mortality. Prevention along with timely and appropriate treatment of these infections is crucial for ICU patients' prognosis.

0018

LOW USEFULNESS OF PCT IN DIAGNOSIS OF BACTERIAL INFECTION IN PATIENTS WITH LIVER CIRRHOSIS

T. Mikula[1], W. Stańczak[1], J. Cianciara[1], A. Wiercińska-Drapało[1]

[1]Warsaw Medical University, Hepatology and AIDS, Warsaw, Poland

BACKGROUND AND AIMS. Procalcitonin (PCT) is a 116 amino acid prohormone of the calcitonin. In severe bacterial infections PCT is synthesized by various cells of liver, lungs, brain and colon. PCT, beside CRP (C-Reactive Protein) is widely used marker of inflammation. In healthy individuals, PCT plasma concentrations in immunoluminometric method (ILMA) are lower than 0.5 ng/ml. CRP normal range is below 10.0 mg/l. The aim of the study was evaluate the value of PCT in comparison with CRP among immunocompromised patients with liver cirrhosis in diagnosis of bacterial infections in patients.

PATIENTS AND METHODS. Clinical symptoms, bacterial or suspected of infections shorter than 3 days were the main including criteria. Blood, urine, cirrhotic fluid cultures, swabs from potentially infected parts of body were taken. The samples for measurement of PCT and CRP were taken once, in the beginning of observation. We evaluated PCT serum concentration in 2 groups cirrhotic patients and group of controls. Group 1 ($n = 48$)—patients with compensated liver cirrhosis, Group 2 ($n = 52$)—decompensated liver cirrhosis and healthy Controls (n = 37). Serum samples of all patients were analyzed with immunoluminometric method (ILMA). The presence of SIRS (Systemic Inflammatory Response Syndrome) were confirmed according the last recommendations. All patients (Table 1) were divided according an advancement of SIRS into 4 groups (No SIRS and no bacterial infections, No SIRS but with presence of bacterial infection, SIRS and Sepsis—severe sepsis and septic shock. Strength of correlation (r) of PCT and CRP serum concentrations were analysed. We confirmed correlation $r > 0.5$ only among patients without SIRS and bacterial infection.

CONCLUSIONS. We suggest low usefulness of PCT immunoluminometric method (ILMA) in diagnosis of bacterial infections in patients with liver cirrhosis. Even in advanced SIRS stages PCT concentrations can be normal. It can be result of use PCT serum concentrations ranges for healthy individuals.

0019

COMPARISON OF PATIENTS WITH PNEUMOCOCCAL AND NON PEUMOCOCCAL PNEUMONIA ON THE INTENSIVE CARE UNIT

H. M. Peet[1], S. Blakeley[1], R. Bowers[1]

[1]Portsmouth Hospitals NHS Trust, Portsmouth, United Kingdom

INTRODUCTION. Five to ten percent of patients with severe community acquired pneumonia (CAP) require admission to the Intensive Care Unit (ICU) [1, 2]. *Streptococcus pneumoniae* is the leading cause of CAP, with predominance in bacteraemic and fatal cases with mortality up to 35%. We sought to review in detail this group of ICU admissions.

METHOD. We retrospectively identified all adult patients admitted to a general ICU with an admitting diagnosis of pneumonia or lower respiratory tract infection, who had a positive isolate of *Streptococcus pneumoniae* or positive urinary antigen over an 18 month period from February 2006. Patients with a diagnosis of pneumonia or lower respiratory tract infection were identified for comparison. Data was collected regarding case mix, outcome and activity for both pneumococcal pneumonia (PP) and non pneumococcal pneumonia (non-PP) admissions. Review of the case notes of those with PP was performed to identify co-morbidities.

TABLE 1 CORRELATION (R) OF PCT TO CRP SERUM CONCENTRATIONS

	Group 1	Group 2	Controls
Number of patients ($n = 137$)	48	52	37
PCT mean serum concentration (ng/ml)	1.47	2.25	0.13
CRP mean serum concentration (mg/l)	35.42	51.76	2.33
No SIRS/no infection	$r = 0.54$	$r = 0.75$	–
No SIRS/infection	$r = 0.41$	$r = 0.63$	–
SIRS	$r = 0.006$	$r = 0.07$	–
Sepsis	$r = 0.24$	$r = 0.17$	–

RESULTS. There were no significant differences in case mix or severity between the 2 groups (Table 1). 37% ($n = 10$) of patients with PP had chronic obstructive pulmonary disease, 37% ($n = 10$) alcohol excess and 29.6% ($n = 8$) ischaemic heart disease. Given the small numbers, no comment can be made regarding the effect of these co-morbidities on outcome.

CONCLUSION. Patients with proven pneumococcal pneumonia accounted for 1.5% of admissions to ICU. The historical excess mortality associated with PP compared to other forms of pneumonia was not seen (ICU mortality 22.2 vs. 25.7%). This may be a reflection of a changing disease process and improving ICU management with emphasis on early introduction of antibiotics and attention to management of severe sepsis.

Patients with pneumococcal pneumonia compared to non-PP are admitted to the ICU sooner after hospital admission and have a longer ICU stay, suggesting they are sicker on presentation to hospital. Despite this no increase in ICU or hospital mortality was seen suggesting that early ICU admission for these patients is beneficial.

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TABLE 1

	All admissions: $N = 1,780$	Pneumococcal pneumonia: $N = 27$	Non pneumococcal pneumonia $N = 179$	P value
Age years: median (range)	64 (0–96)	61 (21–89)	62 (1–86)	NS
Male: n (%)	1,006 (56.5%)	13 (48.1%)	105 (58.7%)	NS
APACHE II score: median (range)	17 (1–53)[a]	20 (12–35)[b]	21 (3–45)[c]	NS
Invasive ventilation: n (%)	1,078 (60.6%)	21 (77.8%)	107 (59.8%)	NS
Duration of ventilation days: median (range)		6 0 (1–15)	4.0 (1–24)	NS
Hospital to ICU admission: median (range); days	1.0 (0–182)	0 (0–11)	2.0 (0–64)	<0.0001
ICU LOS days: median (range)	1.9 (0–88)	9.4 (1–29)	4.2 (0–42.2)	0.01
Hospital LOS days: median (range)	12 (0–285.9)	17.9 (1–79)	18.5 (0.2–115.5)	NS
ICU mortality: n (%)	284 (16.0%)	6 (22.2%)	46 (25.7%)	NS
Hospital mortality: n (%)	417 (23.5%)	7 (25.9%)	59 (33.0%)	NS

[a]$N = 1467$, [b]$N = 27$, [c]$N = 140$ (missing data)
LOS length of stay

0020

DELAY IN EXECUTION AND REMOVAL OF CENTRAL VENOUS CATHETER INCREASES THE POTENTIAL FOR CATHETER RELATED BLOOD STREAM INFECTION

M. P. Vizcaychipi[1], V. Heaviside[2], A. Knight[3], S. Singh[4]

[1]Charing Cross Hospital, Imperial College Academic Healthcare NHS Trust, Anaesthesia and Intensive Care, London, United Kingdom, [2]Bart's and the London NHS Trust, Anaesthesia and Intensive Care, London, United Kingdom, [3]Hillingdon Hospital NHS Trust, Anaesthesia and Intensive Care, London, United Kingdom, [4]Chelsea and Westminster NHS Foundation Trust, Anaesthesia and Intensive Care, London, United Kingdom

INTRODUCTION. There is approximately 6,000 central venous catheter related blood steam infections (CR-BSI) annually reported in the United Kingdom. The majority of CR-BSIs occur in intensive care (1). In 2008 the UK Department of Health introduced a central venous catheter bundle to standardise aseptic central catheter insertion. Our aim was to identify how key clinical decision making can influence the incidence of CR-BSIs.

MATERIAL AND METHODS. This was a prospective observational study registered and approved by the clinical effectiveness committees at Chelsea and Westminster NHS Foundation Trust and Hillingdon Hospital NHS Trust. Data was accrued from critically ill patients admitted to both trusts intensive care units from June 2005 to July 2006.

RESULTS. Forty-one patients were included in this prospective observational study. 24 patients were medical with an average intensive care stay of 16.63 days (3–53 days). Systemic inflammatory response (SIRS) with a CVC in situ was indication for CVC replacement in 15 cases (See Fig. 1). The clinical decision to replace a CVC was made in the morning round in 24 of the cases (Table 1). The insertion of the new CVCs and removal of the old CVCs were performed in the afternoon in 23 and 24 cases, respectively. The average time taken from CVC insertion to radiological imaging was 31 min (02:00 h to 10 min). The average time taken from radiological imaging to review by doctor was 81 min (03:20 h to 11 min). There was an average 3 h 36 min (10:45 h to 15 min) delay from clinical decision to placement of a new CVC. An overlap period of the old and new CVCs of 3 h and 10 min (06:30 h to 10 min) was identified. There was a total delay of 6 h and 27 min (15:25–01:16 h) from clinical decision to removal of the old CVC.

CONCLUSION. In standard practice, when concerns regarding SIRS dictate a central venous catheter change there can be a delay of almost 7 h following this initial clinical decision. To us, the intensivist we seek to find if this is acceptable. Moreover, a delay of almost 3 h from new catheter insertion to removal of old catheter, may provide a targeted outcome measure for improvements in practice.

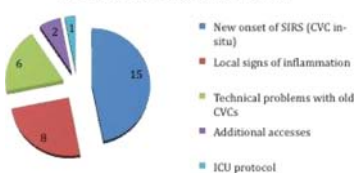

Fig. 1 Indications for removal of old CVCs

TABLE 1 TIME FRAME FOR CLINICAL DECISION

Time frame	AM = Morning (08:00–12:00)	PM = Afternoon (12:01–07:59)
Decision to remove old CVC	10:18 (08:15–12:00)	14:28 (13:00–16:40)
Insertion of new CVC line	11:09 (10:00–12:00)	15:26 (12:30–21:45)
Removal of old CVC	10:40	17:38 (12:30–23:00)

Neuro/emergency medicine 1: 0021–0025

0021

A PHARYNGEAL COOLING SYSTEM IMMEDIATELY DECREASES BRAIN TEMPERATURE WITHOUT CAUSING COLD INJURY IN THE PHARYNX

Y. Takeda[1], K. Shiraishi[1], H. Naito[2], N. Morimoto[2], K. Morita[1]

[1]Okayama University Medical School, Anesthesiology & Resuscitology, Okayama, Japan, [2]Tsuyama Central Hospital, Emergency and Critical Care Center, Tsuyama, Japan

If hypothermia can be initiated immediately after the onset of resuscitation, neurological outcome would be improved. Since bilateral common carotid arteries exist at 1 cm from the pharynx, cooling the pharyngeal region decreases brain temperature by cooling arterial blood without lowering systemic temperature. In the present study, we investigated effects of pharyngeal cooling on brain temperature, tympanic temperature, rectal temperature and mucous membrane in the pharynx in monkeys and in humans.

METHOD 1. Japanese monkeys (7.5 ± 2.4 kg) were divided into a control group ($n = 6$) and a pharyngeal cooling group ($n = 3$) and were anesthetised with 1% isoflurane. Cardiac arrest (12 min) was initiated with electrical stimulation. In the pharyngeal cooling group, a pharyngeal cuff was inserted into the pharynx and was perfused with saline (5°C) at the rate of 500 ml/min from the onset of resuscitation for 30 min. One day ($n = 1$) and 7 days ($n = 2$) after the initiation of pharyngeal cooling, animals were perfuse-fixed for histological evaluation of the mucous membrane of the pharynx.

METHOD 2. Three resuscitated patients (77 ± 10 years) were subjected to pharyngeal cooling for 30 min. Changes in tympanic temperature, bladder temperature, systemic blood pressure and heart rate were monitored. Macroscopic observation of the mucous membrane of the pharynx was performed for 3 days.

RESULTS 1. During cardiac arrest, epidural and sub-cortical temperatures decreased to 33.3 ± 0.7 and 35.8 ± 0.5°C, respectively, in both groups. In the control group, however, epidural and sub-cortical temperatures increased with the initiation of resuscitation and reached 35.1 ± 0.5 and 36.5 ± 0.2°C, respectively, 30 min later. In the pharyngeal cooling group, epidural and sub-cortical temperatures decreased and reached 31.1 ± 1.5 and 32.4 ± 1.3°C, respectively, 30 min later. Rectal temperature was unchanged in both groups. Microscopic observation (HE staining) showed that mucous membranes of the pharynx were intact. No inflammatory cell infiltration was observed

RESULTS 2. Tympanic temperature (36.3 ± 1.2°C) was decreased to 35.7 ± 1.0°C 30 min after initiation of pharyngeal cooling. Bladder temperature (36.3 ± 0.9°C), mean arterial blood pressure (90 ± 16 mmHg) and heart rate (90 ± 24/min) were unchanged at 30 min after initiation of pharyngeal cooling (Bladder temperature, 36.3 ± 1.0°C; mean arterial blood pressure, 96 ± 18 mmHg; and heart rate, 93 ± 21/min). Edema formation or inflammatory findings, suggesting development of cold injury, were not observed in the pharyngeal mucous membrane for 3 days.

CONCLUSIONS. Brain temperatures were decreased by the initiation of pharyngeal cooling without any effect on rectal temperature, blood pressure and heart rate in monkeys and in humans. Since the mucous membrane in the pharynx was intact after 30 min of cooling, pharyngeal cooling could be a useful technique for protecting the brain from ischemic injury in a clinic.

0022

REFRACTORY STATUS EPILEPTICUS: APPROACH AND MANAGEMENT IN A NEUROLOGICAL INTENSIVE CARE UNIT

O. H. Hernandez[1], J. F. Zapata[2], A. Franco[2], M. Jimenez[2], M. Massaro[3], A. Guerra[1], J. C. Arango[1], J. D. Ciro[1], C. S. Uribe[1], J. I. Suarez[4]

[1]Instituto Neurologico de Antioquia, Neurological Intensive Care Unit, Medellin, Colombia, [2]Instituto Neurologico de Antioquia, Clinical Neurophysiology Unit, Medellin, Colombia, [3]Instituto Neurologico de Antioquia, Research and Education Department, Medellin, Colombia, [4]Baylor College of Medicine, Department of Vascular Neurology and Neurocritical Care, Houston, United States

INTRODUCTION. Refractory status epilepticus (RSE) constitutes a medical emergency with a significant morbidity and mortality. Management of RSE requires an accurate diagnosis and a rapid and aggressive treatment to successfully stop it. RSE is defined as status epilepticus refractory to first- and second-line medications requiring general anesthesia.

OBJECTIVES. To describe the management approach of RSE in a neurological intensive care unit (NICU).To assess the outcomes of these patients according of type of RSE and the response to treatment.

METHODS. We conducted a retrospective study over 15 months (09/2007–12/2008) of RSE patients. The pharmacologic treatment was guided by continuous video EEG monitoring (CVEEGM). We collected the following information: patients' demographics, etiology of RSE, APACHE II score, clinical characteristics of seizures, EEG findings, treatments and short term outcomes. We defined EEG control of the RSE as burst suppression pattern or a decrease in the ictal activity. We performed descriptive statistics and compared proportions using Chi-square or Fischer's exact test as appropriate.

RESULTS. We included 80 patients with RSE. Of those, 75% had non-convulsive RSE; 51.3% were male; their mean age was 45 years; and 52.5% of them had an APACHE II score ≥15. The etiology of RSE was a neurological lesion in 75.1% (48.3% stroke, 15% infection, 13.5% trauma, 23.4% other), underlying epileptic disease in 20% and systemic abnormalities in 4.9% of patients. Our treatment included general anesthesia (continuous infusions of midazolam, propofol and/or thiopental) and concomitant anticonvulsivants (valproic acid, levetiracetam, topiramate and phenobarbital, among others) in 78.8% of patients. RSE was successfully controlled within 3 days in 87.5% of patients. The EEG patterns during treatment induction were as follows: focal electrographic seizure activity (80%); periodic discharges (95%) and pseudoperiodic discharges (40%). The mean follow up with CVEEGM was 138 ± 73.6 h. In-hospital mortality was 22.5%. At 1-month follow up, 48.4% of patients had regained their independent activities of daily living. The clinical and EEG features did not affect the RSE length of treatment, length of NICU stay, RSE control and discharge condition. Patient survival and modified Rankin scale ≤2 correlated positively with RSE control achievement (82.9 vs. 40%, *P* 0.008; 63.6 vs. 22.2%, *P*: 0.003, respectively).

CONCLUSIONS. RSE is a medical emergency. ICU management of RSE by a team of neurointensivists, neurophysiologists and neurologists, guided under CVEEG monitoring, permits a rapid and adequate control of these patients to improve short term prognosis.

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0023

EFFECT OF ANALGO-SEDATION PROTOCOL FOR DANISH NEUROINTENSIVE PATIENTS

I. Egerod[1], M. Brorsen[2], S. Herling[2], K.-L. Welling[2]

[1]University of Copenhagen, Health Sciences, Copenhagen O, Denmark, [2]Copenhagen University Hospital Rigshospitalet, 2093, Copenhagen, Denmark

AIMS. The aim of the study was to assess the effect of a sedation protocol for neurointensive patients based on the principles of analgo-sedation. The primary objectives were a shift from sedation-based to analgesia-based sedation (analgo-sedation) and a reduction in pain level. Intensive care patients usually require sedation and analgesia in order to maintain comfort, relieve anxiety, facilitate care, and adapt to ventilatory support. A recent trend in sedation management is analgo-sedation, wherein the patient is primarily treated for pain, and, if necessary, sedated. Guidelines have been developed for general intensive care patients resulting in shorter duration of mechanical ventilation, shorter hospital stay, and fewer incidences of ventilator associated pneumonia. Only few sedation protocols for neurointensive patients exist, due to the difficulty in assessing the pain and sedation levels and to the need to maintain adequate cerebral perfusion pressure, mean arterial pressure, and control intracranial pressure.

METHODS. The design was a prospective two-phased single-center before-after study at a 14-bed NICU at a 1,082-bed university hospital in Denmark. Patients were consecutively enrolled in the study during two 7-month periods in January through July 2007 ($n = 106$) and April through October 2008 ($n = 109$). Patients were included if they were ≥18 years old, admitted to the NICU and intubated within 24 h, mechanically ventilated and requiring continuous infusions of sedatives and analgesics. Patients were excluded if they were potential organ donors, non-sedated, non-intubated, or transferred intubated from other units.

RESULTS. The before and after groups were similar in sex, age, weight, APACHE II, SAPS II, SOFA, and admission diagnosis. Hospital stay, NICU stay, duration of mechanical ventilation, incidence of late pneumonia, and accidental extubation were also unchanged, but the duration of sedation was significantly reduced from 125 to 112 ($P = 0.038$) mean hours of sedation. The sedation level (Ramsay 4) and the Glasgow Coma Score, GCS (8 during sedation breaks) were unchanged, but the pain intensity score was significantly reduced from 1.54 to 1.24 ($P < 0.000$). The medication pattern shifted from sedative to analgesic infusions; there was a significant reduction in the daily dose of propofol and midazolam, and a significant increase in the daily dose of fentanyl, remifentanil.

CONCLUSIONS. The study confirms the feasibility of targeting issues of pain management in the neurointensive population as a sedation protocol decreases the variability of practice and increases staff awareness. Better assessment methods are still needed to distinguish among levels of pain, sedation, drug accumulation and decreased level of consciousness.

0024

FIBRINOGENOLYSIS DURING THE EARLY STAGE OF TRAUMA PREDICTS THE OCCURRENCE OF MASSIVE BLEEDING IN PATIENTS WITH BLUNT TRAUMA

M. Hayakawa[1], T. Wada[1], K. Katabami[1], M. Sugano[1], N. Henzan[1], H. Hoshino[1], A. Sawamura[1], S. Gando[1]

[1]Hokkaido University Hospital, Emergency and Critical Care Center, Sapporo, Japan

INTRODUCTION. Several reports have so far indicated that the main pathophysiology of the coagulopathy associated with the early stage of trauma is fibrinolysis, but not the significant consumption of coagulation factors. FDP consists of both fibrin degradation (fibrinolysis) products and fibrinogen degradation (fibrinogenolysis) products. However, D-dimer consists of fibrin degradation products, but excluding fibrinogen degradation products. In other words, a high level of FDP without a D-dimer elevation indicates a state of fibrinogenolysis.

OBJECTIVE. We hypothesized that the levels of FDP and D-dimer on the admission could help to predict the necessity to perform an aggressive transfusion of coagulation factors by evaluating the balance of fibrinogenolysis and fibrinolysis in blunt trauma patients. We investigated the characteristics of coagulopathy during the early stage of trauma, and thus identified the predictive parameters for massive bleeding.

METHODS. Eighty-three blunt trauma patients enrolled in the study and 182 patients with sepsis were selected as a control group. The clinical backgrounds of the patients and the measured variables were all retrospectively collected.

RESULTS. On admission, the FDP and D-dimer levels increased in the trauma patients much more than in the patients with sepsis. The figure shows the D-dimer/FDP % and the levels of D-dimer and FDP in each group. The FDP and D-dimer levels markedly decreased from admission to 24 h after admission. In the trauma patients, the D-dimmer/FDP % on admission rapidly increased to the same percentage as that observed in patients with sepsis. In an ROC curve analysis for the risk of massive transfusion, FDP showed a large AUC among the various coagulation tests. The best cutoff point for FDP as an indicator for the risk of massive transfusion was 64.1 μg/ml with a sensitivity of 76.9% and a specificity of 73.1%, and these values were the same as when the cutoff point for D-dimmer/FDP % was 52.9%.

CONCLUSION. 1. In comparison to the patients with sepsis, more intense hyper-fibrinolysis and fibrinogenolysis were observed in the early stage of trauma in the blunt trauma patients;. 2. the fibrinogenolysis during the early stage of trauma was promptly suppressed to same level as that observed in the patients with sepsis;. 3. the elevation of FDP and the low percentage of D-dimer/FDP % thus indicated the presence of fibrinogenolysis and predicted the necessity to perform massive transfusions (Fig. 1).

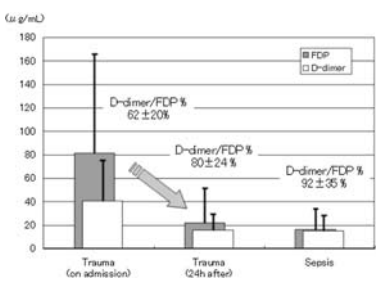

Fig. 2 The change of the fibrinogenolysis

0025

RAPID REVERSAL OF COAGULOPATHY IN WARFARIN-RELATED INTRACRANIAL HEMORRHAGES WITH PROTHROMBIN COMPLEX CONCENTRATES (PCC)

C. T. Chong[1], T. W. Lew[1], P. Kuperan[2], J. Tan[1], H. L. Tan[1], T. K. Kwek[1]

[1]Tan Tock Seng Hospital, National Healthcare Group, Anaesthesiology, Singapore, Singapore, [2]Tan Tock Seng Hospital, National Healthcare Group, Laboratory Medicine, Singapore, Singapore

INTRODUCTION. Intracranial hemorrhage is a life-threatening complication that occurs during warfarin oral anticoagulant therapy (OAT) with mortality in excess of 50%. Early hematoma growth is a known predictor of poor outcome [1]. Patients presenting with OAT-related intracranial hemorrhage thus mandate rapid PT/INR normalization to decrease the risk of early hematoma enlargement and to facilitate early neurosurgical evacuation when indicated.

METHODS. We reviewed all consecutive patients with OAT-related intracranial hemorrhage admitted to our acute tertiary-level NICU and treated with PCC from January to June 2008. All patients were on warfarin OAT for clinically appropriate indications, had INR >1.5 at presentation with CT diagnosis of intracranial hemorrhage. In consultation with the hematologist, *Profilnine* SD (Grisols Biologicale Inc, Los Angeles, USA), a 3-Factor PCC containing per 100 U of factor IX, 148 U of factor II, and 64 U of factor X, was administered with FFP (as an adjunct source of Factor VII) and Vitamin K.

RESULTS. A total of seven patients received PCC for OAT-related intracranial hemorrhage during the 6-month period. Most of the patients had admission INR within or close to therapeutic range of 2–3, except for one patient whose INR was 7.74.

The majority of intracranial bleeds were subdural hematomas (4/7 patients or 57%), with significant deterioration in conscious level (GCS 3–9) requiring urgent surgical evacuation. The mean maximum diameter of the SDHs in four patients was 18.1 mm (range 11.5–33 mm). The mean maximum diameters of intracerebral bleeds in three patients were 45.3 mm (range 15–61 mm). The dose of PCC administered ranged from 1,000 to 3,000 IU (equivalent to a median of 28.5 IU/kg body weight (range 14.9—63.8 IU/kg)). All four patients with SDH underwent surgical evacuation once INR was <1.5. Median time from CT diagnosis to surgery was 275 min (range 102–420 min).

Four of seven patients had good neurological outcome (GOS 4) at 30 days. The median time to INR normalization post-PCC administration was shorter at 85 min (range 50 min to 7 h) for the four patients that survived, in contrast to the three patients that died (median time 10 h, range 9–44 h). Two of the three patients who died had CT evidence of hematoma growth, worsening midline shift and subfalcine herniation.

CONCLUSIONS. PCC should be considered for use in the urgent reversal of OAT-related intracranial hemorrhage, potentially halting hematoma expansion and expediting urgent neurosurgery, although randomized trials are lacking [2]. A protocolized emergent treatment algorithm is proposed and may achieve earlier consistent normalization of INR.

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Resource consumption in ICU: 0026–0030

0026

THE INCIDENCE OF SEVERE SEPSIS: THE INFLUENCE OF DEFINITIONS

P. J. Watkinson[1], S. M. Drage[2], V. S. Barber[1], S. Lowes[2], J. D. Young[1]

[1]University of Oxford, Intensive Care Society Trials Group, Oxford, United Kingdom, [2]Brighton and Sussex University Hospitals NHS Trust, Intensive Care, Brighton, United Kingdom

INTRODUCTION. Consensus Conference [1] and PROWESS study [2] criteria have become the standard definitions upon which most studies of severe sepsis in intensive care units (ICUs) are based. These definitions require evidence of infection and abnormalities in physiological variables that define the SIRS (systemic inflammatory response syndrome) and organ failure components of severe sepsis. These abnormalities can be present, even transiently, at any point in the previous 24 h to make the diagnosis. However, clinicians tend to make a clinical diagnosis of severe sepsis if all or most the abnormalities are present simultaneously. It is unknown whether these differing definitions can explain the discrepancy between the incidence of severe sepsis in observational studies and recruitment rates to trials of agents for the treatment of severe sepsis. This study investigated the effect of the timing of SIRS and organ failure criteria on the incidence of severe sepsis. It also assessed whether the use of two (original Consensus Conference definition) or three (PROWESS study) SIRS criteria altered the incidence of severe sepsis.

OBJECTIVES. To quantify the effect of different definitions on the incidence of severe sepsis.

METHODS. An observational study was carried out within a randomised controlled trial in three ICUs in England. 1,002 consecutive patients were screened each morning at 1,000 h. Any infective diagnosis was recorded. Organ failure and SIRS criteria were determined from the most current data and from data at anytime within the previous 24 h.

RESULTS. The incidence of sepsis in the first 24 h following admission varied from 26.4% of admissions if the PROWESS study criteria were used with the most recent results, to 37.3% if the Consensus Conference criteria were used with the most extreme values in the previous 24 h. The prevalence of severe sepsis (proportion of patient days when patients met the criteria) varied from 18.5% (PROWESS study criteria, most recent values) to 46.9% (Consensus Conference criteria, 24 h values). Two SIRS criteria were present in a 24 h period in 91% of patients, and no patient simultaneously had three SIRS criteria without infection.

CONCLUSIONS. Severe sepsis, far from being a clear clinical entity, has an incidence heavily dependent on the diagnostic criteria. Identifying suitable patients for trials of specific treatments using techniques so sensitive to timing and a difference of one variable may recruit the wrong subjects. The different criteria used in epidemiological studies of severe sepsis may partially account for the differing reported incidences.

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0027

VANCOMYCIN ADMINISTRATION DOES NOT INCREASES HEMODIALYSIS-HEMOFILTRATION REQUIREMENTS MORE THAN OTHER ANTIBIOTICS USED IN SEVERE SEPSIS

J. Massaut[1], O. Noordally[2], F. Corrazza[3], P. Reper[2]

[1]U.L.B, Intensive Care, Bruxelles, Belgium, [2]CHU Brugmann, Intensive Care, Bruxelles, Belgium, [3]CHU Brugmann, Laboratory, Bruxelles, Belgium

INTRODUCTION. Potentially nephrotoxic antibiotics have been incriminated as causes of increased need of hemodialysis in intensive care patients based on historical evolution [1].

OBJECTIVES. To evaluate the incidence of vancomycin administered as continuous intravenous infusions on hemodialysis needs in our intensive care we reviewed the evolution of 1,263 consecutives patients and analyzed the effect of all antibiotics treatments on hemodialysis–hemofiltration (HH) requirements.

METHODS. We analyzed the data stored in our intensive care data management system [2] updated with laboratory data to systematically review all the antibiotic administrations and the creatinine blood level during these treatments and their relations to consecutive needs of HH. Data were analyzed by univariate and multivariate logistic regression. *P* values <0.05 were considered as significant. Variables significantly linked to HH at the univariate analysis were entered in the multivariate logistic regression. For statistical analysis, we used Stata 8 for UNIX. Target for vancomycin infusion was between 20 and 35 mcg/ml.

RESULTS. Thirty-seven patients of 1,263 (2.9%) received HH. 549 (19.71%) patients received antibiotics. Vancomycin, Meropenem, Piperacilin-Tazobactam, Fluconazole treatments and creatinine blodd levels above 2 mg/dL during treatment were significantly associated with the necessity of HH, but LROC values, respectively, of 0.53, 0.53, 0.56, 0.54 for these treatments were very low compared to LROC values of 0.75 for creatinine above 2 mg/dL. Table 1 shows odds ratios, *P* values and confidence interval for the multivariate analysis.

TABLE 1 MULTIVARIATE ANALYSIS

	Odds Ratio	*P* value	95% CI high	95% CI low
Vancomycin	5.21	0.001	1.92	14.12
Meropenem	5.78	0.002	1.93	17.30
Pipe-Tazo	3.47	0.001	1.60	7.37
Fluconazol	5.67	0.001	1.94	16.55
Creatinine >2 mg/dL	16.74	0.001	2.99	93.57

DISCUSSION. Vanmycin administration is significantly associated to the need of HH at the univariate and multivariate analysis, but this is also true for other antibiotics not known as nephrotoxic and used in severe sepsis. Odds ratio for vancomycin at the multivariate analysis is not different from odds ratio for meropenem and Piperacilin-Tazobactam and may reflect an association and not a cause effect relationship.

CONCLUSIONS. Based on our data from 1,263 intensive care consecutive patients, vancomycin administration does not increases HH requirements more than other antibiotics used in severe sepsis.

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0028

COST ANALYSIS OF COMPUTER-ASSISTED GLUCOSE REGULATION PROGRAM IN THE INTENSIVE CARE UNIT

M. Hoekstra[1], K. Vermeulen[2], M. Vogelzang[3], I. C. C. van der Horst[3], J. van Pelt[4], F. Zijlstra[3], E. Buskens[2], M. W. N. Nijsten[5]

[1]University Medical Center Groningen, Departments of Anesthesiology and Cardiology, Groningen, Netherlands, [2]University Medical Center Groningen, Department of Epidemiology, Groningen, Netherlands, [3]University Medical Center Groningen, Department of Cardiology, Groningen, Netherlands, [4]University Medical Center Groningen, Department of Laboratory Medicine, Groningen, Netherlands, [5]University Medical Center Groningen, Department of Intensive Care, Groningen, Netherlands

INTRODUCTION. As recommended by recent guidelines, glucose control (GC) has been implemented in many ICU's. Several studies have hinted that GC is associated with considerable costs. In our ICU glucose is regulated by a nurse-driven computerized clinical decision support system that was designed to improve patient safety and optimize glycaemic control [1].

OBJECTIVE. To determine the costs of GC as performed by a computerized protocol using point-of-care blood glucose measurements.

METHODS. We comprehensively analyzed all the costs of (computer-assisted) glucose regulation in a mixed ICU (45 beds) in a regional university teaching hospital that covers all adult patient specialties. The effectiveness of GC was determined in terms of achieved glucose levels and incidence of severe hypoglycaemia (glucose <2.2 mmol/L).

RESULTS. The variable costs of glucose management (including personnel costs) were €7.88 per point-of-care measurement, the fixed costs were €4.68 per patient per day. For our ICU the total costs of glucose regulation with 5.6 point-of-care glucose measurements per patient per day were €48.80. In an alternative scenario where the regulation program would use more frequent glucose measurements, as the majority of published glucose regulation protocols do (i.e. 12–18 measurements/day), this sum increases to €100–€150 per patient per day. In 5,898 consecutive ICU patients glucose regulation was effective with the blood glucose within the predefined target range (4.0–7.5 mmol/L) in two-thirds of the time. Severe hypoglycaemia was uncommon (0.05% of measurements <2.2 mmol/L, 1.0% of patients experienced an episode <2.2 mmol/L). No mortality or morbidity could be related to hypoglycaemia.

CONCLUSION. Glucose control, as achieved with the assistance of an effective and efficient computer-assisted program, costs an estimated €50 per day per ICU patient. Altogether, including 35% overhead costs, for our institution (45 beds) this leads to approximately €1.100.000 per year. The major cost-determining factor was the number of point-of-care glucose measurements per day. Compared to other published computerized glucose protocols, using more frequent measurements, our institution achieved major absolute and relative cost savings (approximately 50%) by applying 5.6 measurements per day. However, even with a system designed to optimize GC, costs are considerable.

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0029

ROUTINE AND ON-DEMAND PRESCRIPTION OF CHEST RADIOGRAPHS IN MECHANICALLY VENTILATED ADULTS: A MULTICENTER CLUSTER-RANDOMIZED TWO-PERIOD CROSS-OVER STUDY

B. Guidet[1], G. Hejblum[2], L. Chalumeau-Lemoine[3], V. Ioos[3], C. E. Luyt[3], J. L. Diehl[4], L. Salomon[5], T. Simon[6], E. Schouman-Claeys[7], RARE

[1]UFR Saint Antoine, Réanimation Médicale, Paris, France, [2]U707, INSERM, Paris, France, [3]Paris VI, Réanimation Médicale, Paris, France, [4]Paris V, Réanimation Médicale, Paris, France, [5]Paris VII, Santé Publique, Colombes, France, [6]Paris VI, URC Est, Paris, France, [7]Paris VII, Radiology, Paris, France

BACKGROUND. Current guidelines recommend *Routine* daily chest radiographs (CXRs) for mechanically ventilated patients in intensive care units (ICUs). However, some ICUs have shifted to an *On-demand* strategy, in which this CXR is only prescribed if warranted by the patient's status at the morning physical examination. Here we compared *Routine* and *On-demand* strategies in 21 French ICUs. The working hypothesis was that CXR prescriptions would fall by at least 20% with the *On-demand* strategy, with no reduction in quality of care.

METHODS. Based on a cluster-randomized two-period two-strategies cross-over design, respectively, 11 and 10 participating ICUs applied the *Routine* and *On-demand* strategies during the first period, each enrolling 20 consecutive patients requiring mechanical ventilation for at least 2 days. Each ICUs applied then applied the alternative strategy during the second period, again enrolling 20 consecutive patients.

FINDINGS. Respectively 424 and 425 patients received 4,607 and 3,148 CXRs with the *Routine* and *On-demand* strategies, representing a reduction of 32% with the *On-demand* strategy ($P < 10^{-6}$). Similar numbers of CXRs (respectively 728 and 729) led to therapeutic or diagnostic interventions. The two strategies were associated with similar mean durations of mechanical ventilation (9.82 and 9.84 days) and ICU stay (13.96 and 13.21 days), and similar ICU mortality rates (30.9 and 32.0%).

INTERPRETATION. An *On-demand* prescription strategy reduces CXR consumption with no measurable change in quality of care.

0030

COST-EFFECTIVENESS OF THE SURVIVING SEPSIS CAMPAIGN IN SPAIN

R. Ferrer[1], Edusepsis Study Group

[1]Sabadell Hospital. CSPT. UAB. CIBER-ER., Sabadell, Spain

INTRODUCTION. In Spain, a multicenter (59 ICUs) prospective before and after educational study (Edusepsis, Ferrer et al. JAMA 2008) based on the Surviving Sepsis Campaign (SSC) was able to improve care and reduce mortality.

OBJECTIVE. To compare in terms of cost-effectiveness the protocol of the SSC in Spain for the treatment of severe sepsis after the implementation of a multicentre educational program with the conventional care of severe sepsis.

METHODS. Post hoc cost-effectiveness analysis. Costs and effectiveness were calculated in the preintervention and the postintervention cohorts. Calculation of costs was done from the health care system perspective, costs were not discounted and timeline horizon was from sepsis onset to hospital discharge. Calculation of effectiveness: Life-Years Gained (LYG) and Quality Adjusted Life Years (QALYs). The age and gender specific life expectancy for each hospital survivor was estimated using "2005 Mortality tables. National Institute of Statistics, Spain". The previous life expectancy was adjusted by 0.51, the estimated life reduction for sepsis survivors (Quartin et al. 1997) to obtain the LYG. LYG were adjusted by a utility weight of 0.69 to get the QALYs (Davies et al. 2005). The end-points of the study were: Incremental Cost-Effectiveness Ratio (ICER) and Incremental Cost-Utility Ratio (ICUR).

RESULTS. Cost and effectiveness data from the preintervention and the postintervention cohort are shown in Table 1.

TABLE 1 COST AND EFFECTIVENESS RESULTS

	Preintervention cohort ($n = 854$)	Intervention cohort ($n = 1465$)
Length of Stay, days		
ICU	12.6 (16.4)	13.7 (18.1)
Ward	11.0 (16.9)	12.7 (18.3)
Overall	23.6 (25.6)	26.4 (27.7)
Costs, 2006 Euros	16937.1 (19042.6)	18726.9 (21082.6)
Mortality, *n* (%)	376 (44.0)	580 (39.6)
LYG	6.7 (8.2)	7.4 (8.3)
QALYs	4.6 (5.6)	5.1 (5.7)

Main costs were related to hospital stay. The ICER per LYG was 2556.9€ and the ICUR per QALY was 3579.6€.

CONCLUSIONS. The ICER of the SSC in Spain was less than 30.000€/LYG. Therefore, it is a cost-effectiveness intervention.

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